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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,277	04/13/2001	Andrea D. Branch	RII-003CPUS	7039

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EXAMINER	
BROWN, TIMOTHY M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 01/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,277	BRANCH ET AL.	
	Examiner	Art Unit	
	Tim Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2004 and 01 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-58* is/are pending in the application.

4a) Of the above claim(s) *50,51,54 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-49,52,53,55,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Final Office Action is responsive to the Amendments mailed January 5, 2004 and June 1, 2004. Claims 31-37 have been canceled by Applicant. Claims 38-58 are pending. Claims 50, 51, 54 and 56 are withdrawn from consideration as being directed to a non-elected invention.

Applicant asserts that all the pending claims should be examined according to Applicant's election of Group VIII (i.e. a method for detecting an HCV +1 reading frame polypeptide; see response mailed September 26, 2002). Applicant asserts that claims drawn to a method for detecting antibodies against an HCV +1 reading frame polypeptide should be rejoined because they fall within the scope of an allowable linking claim (i.e. claim 52). The Examiner respectfully disagrees.

First, neither claim 52, nor any claim having the scope of claim 52, has been indicated as allowable. Second, claim 52 is not a linking claim. A linking claim is a claim having a Markush group that (1) shares a common utility, and (2) shares a substantial structural feature disclosed as being essential to that utility. See *In re Harnish,* 631 F.2d 716 (CCPA 1980). Claim 52 is for a method of detecting an HCV infection comprising detecting (1) a *polypeptide* having the amino acid sequence of an HCV ARF polypeptide ("ARF"), (2) a *polypeptide* that is recognized by an antibody against an HCV ARF polypeptide, or (3) an *antibody* against an ARF polypeptide. Claim 52 fails the second linking claim requirement. Although the claimed polypeptides and claimed antibody share a common utility (i.e. diagnosing HCV), they do not share a structural feature that contributes to this diagnostic utility. The utility of Applicants'

polypeptide relies on its specific sequence and conformation which provides a unique epitope for antibody recognition. In contrast, the diagnositic value of the claimed antibody is derived from a Fab fragment comprised of heavy and light chain CDR loops which confer specific antigen recognition. Because the claimed peptides and antibody do not share a common structural feature, claim 52 is not a linking claim that requires rejoinder of claims 50, 51, 54 and 56.

Claim Objections

Claim 52 is objected to for failing to define the acronym "HCV." Amending the claim to recite "Hepatitis C Virus (HCV)" would overcome this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52, 53, 57, 58 and 38-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. Applicants' invention is drawn to a method for detecting HCV infection comprising detecting an epitope from an HCV ARF polypeptide. The invention does not include the critical steps of introducing a sample, incubating the

sample to obtain a detectable complex, or correlating the detected complex with HCV infection. The state of the art continues to require these steps at a minimum. This is consistent with Applicants' own specification which describes diagnosing HCV infection using cells, or body fluid, collected from a subject (p. 30, lines 1-10). Applicants' specification does not however disclose how to detect HCV infection in the absence of a sample, an incubation step, and an association step wherein a result is correlated with infection. Thus, the specification does not enable one of ordinary skill in the art to use the claimed invention.

Even if independent claim 52 were amended to include the steps noted above, the full scope of the invention would still lack enablement. This results because the invention diagnoses HCV based on the detection of any and all immunogenic HCV ARF peptides. While the specification identifies a limited number of ARF polypeptides, it does not teach all of those which are immunogenic. Moreover, the number of potentially immunogenic ARF polypeptides is large given that an HCV epitope can be as small as six amino acids and that there are over 9,000 bases in the HCV genome. As noted above, one skilled in the art would have to perform undue experimentation to identify the full range of ARF polypeptides claimed. Therefore, the specification fails to enable the full scope of the invention.

Independent claim 52 also lacks enablement in that it is not clear that detecting any and all HCV ARF polypeptides would serve to identify HCV infection. This is because there is no evidence that the full range of HCV polypeptides detected by Applicant's method are in fact expressed in the serum of individuals infected with HCV.

Therefore, Applicant's specification fails to enable the detection of HCV using the full range of antibodies claimed.

Claims 57, 58, 39, 40 and 42-45 also lack enablement in that they are drawn to a broad range of amino acid sequences that do not necessarily react with anti-HCV antibody. For example, claim 57 is drawn to any amino acid sequence that is "at least about 60% to 70% identical to . . . SEQ ID NO:2 over at least about 30-40 amino acids." It is clear that not every HCV peptide is capable of inducing an immune response that produces a specific anti-HCV antibody. Research by Rodriquez-Lopez et al. found that only 179 out of 543 synthetic HCV polypeptides were recognized by serum from HCV-infected individuals (Journ. of Gen. Virol. (1999) 80, 727-738, see p. 732). Thus, one of ordinary skill in the art could not possibly predict which of the claimed peptides claimed would actually react with anti-HCV antibody. Applicants' working examples are no less helpful in this regard; Applicants failed to produce a single assay wherein an ARF polypeptide is detected, let alone the broad range of peptides claimed. Thus, in order to practice the invention, one of ordinary skill would be forced to produce a library of HCV peptide clones, scale up each clone for the production of peptides, determine whether the peptides are capable of inducing an immune response, and determine whether the peptide is in fact expressed in infected individuals. Clearly, such experimentation is undue. Therefore, Applicant's specification does not enable diagnosing HCV infection using the claimed polypeptides.

Claims 52, 53, 55, 57, 58 and 38-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention lacks enablement for two reasons. First, as noted above, Applicants' specification does not disclose a method for diagnosing HCV infection that omits the steps of introducing a sample, incubating the sample to obtain a detectable complex, and correlating the detected complex with HCV infection. Second, the specification does not disclose the full range of ARF polypeptides claimed. The invention is drawn to diagnosing HCV based on the detection of any and all immunogenic HCV ARF polypeptide. However, the specification only discloses a limited number of purportedly immunogenic amino acid sequences. Thus, the specification lacks written description of the HCV ARF polypeptides that are claimed. For at least these two reasons, the specification does not establish that Applicants possessed the invention at the time the application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52-55 and 38-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 52 is indefinite for omitting essential steps. Claim 52 is a method for diagnosing HCV infection comprising detecting an immunogenic polypeptide. However, diagnosing HCV based on the presence of an immunogenic polypeptide at least requires 1) collecting a sample from an individual suspected of being infected with HCV, 2) introducing the sample to a reaction mixture that permits detection of the immunogenic polypeptide, and 3) correlating the detection of the immunogenic polypeptide with HCV infection. It is unclear how the claimed method could diagnose HCV infection absent these steps. Accordingly, claim 52 is indefinite for omitting essential steps.

Claim 52 is also indefinite in the recitation of "a polypeptide comprising . . . an HCV alternate reading frame polypeptide." This limitation is indefinite because it is unclear which polypeptides are encoded by such a reading frame. Since the polypeptide "comprises" and alternate reading frame polypeptide, does the claimed invention also include missense, non-sense and/or silent mutations? One skilled in the art would not be able to appreciate the metes and bounds of the claimed invention.

Claim 57 is indefinite in the recitation of "60% to 70% identical to *a polypeptide sequence* shown in SEQ ID NO:2." It is unclear whether "a polypeptide" refers to a polypeptide consisting of, or comprising, SEQ ID NO:2.

Claims 57, 58, 39, 40, 42 and 43 are indefinite in the recitation of "at least about." For example, claim 58 recites "wherein the amino acid sequence is at least about 100 amino acids in length." The specification does not provide any guidance to the scope of "at least about." Moreover, the level of skill in the art does not provide any clarity as to

Applicants' use of "at least about." Thus, claims 57, 58, 39, 40, 42 and 43 fail to particularly point out and distinctly claim the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 52, 53, 55, 58, 38-41 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Lo (Lo, S. *Differential Subcellular Localization of Hepatitis C Virus Core Gene Products* Virology (1995) No. 213, 455-461).

Despite the lack of clarity noted above, the claims are interpreted as being drawn to an immunoassay for diagnosing HCV infection comprising detecting an HCV ARF polypeptide using an antibody that is specific for an HCV ARF polypeptide. Lo anticipates the claimed invention because it teaches detecting P16 and other HCV core polypeptides using Western blot analysis (p. 457, esp. Fig. 1). Although Lo did not disclose P16 as an ARF polypeptide *per se*, later research revealed that Lo's P16 was in fact an HCV ARF polypeptide (Xu, Z. EMBO (2001) Vol. 20, No. 14, 3840-3848). Thus, by teaching the detection of P16 using Western blot analysis, Lo anticipates the claimed invention.

It should be noted that Lo also teaches detecting "a polypeptide comprising an amino acid sequence of an HCV ARF polypeptide that is immunoreactive with an

antibody that is specifically binds to an HCV ARF polypeptide." This results because P16, which is an ARF polypeptide, would inherently have the ability to interact with any antibody that is specific for it.

Claims 52 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Feucht (Feucht, H.H. *Study on Reliability of Commercially Available Hepatitis C Virus Antibody Tests* Journ. Of Clin. Microb. (1995) 620-624).

Claims 52 and 57 are interpreted as being drawn to an immunoassay for diagnosing HCV infection comprising detecting an HCV ARF polypeptide using an antibody that is specific for an HCV ARF polypeptide, wherein the HCV ARF is 60% to 70% identical to *a* polypeptide sequence shown in SEQ ID NO:2. Feutch anticpates the claimed invention in that it teaches the serodiagnosis of HCV-infected individuals comprising detecting a protein that is 60% to 70% identical to *a* polypeptide sequence shown in SEQ ID NO:2 (see eg. Fig. 1 and Table 2).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tim Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

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